

## **REMARKS**

In the Office Action mailed September 17, 2008 the Examiner rejected Claims 26-27, 29-31, 33-35 and 38-46 as allegedly being unpatentable over Claims 1-2, 8-10, 22-23 and 27 of U.S. Patent No. 6,471,968 (hereinafter "the '968 patent") in view of Tomalia et al., Agnew Chem. Int. Ed. Engl. 29, 138-175 (1990) (hereinafter, "the Tomalia reference"), as further evidenced by Zhou et al., J Controlled Release (1999) (hereinafter, "the Zhou reference"), and rejected Claims 26-35 under 35 U.S.C. § 103(a) as allegedly being unpatentable over the Tomalia reference and the Zhuo reference in view of Malik et al. (Proceed. Int'l Symp. Control. Rel. Bioact. Mater., 24: 107-108 (1997); hereinafter "the Malik reference"), U.S. Patent No. 5,714,166 (hereinafter "the '166 patent") and U.S. Patent No. 6,221,959 (hereinafter "the '959 patent"). Each rejection is addressed below.

### **I. Nonstatutory Obviousness-Type Double Patenting**

The Examiner rejected Claims 26-27, 29-31, 33-35 and 38-46 as allegedly being unpatentable over Claims 1-2, 8-10, 22-23 and 27 of the '968 patent in view of the Tomalia reference.

The Applicants respectfully disagree. Nonetheless, in order to expedite prosecution without acquiescing to the Examiner's arguments, the Applicants herein submit with this Response a Terminal Disclaimer with regard to the '968 patent, thereby rendering this rejection moot.

### **II. The Amended Claims are Not Obvious**

The Examiner rejected Claims 26-35 and 47-50 under 35 U.S.C. § 103(a) as allegedly being unpatentable over the Tomalia reference and the Zhou reference in view of the Malik reference, the '166 patent, and the '959 patent. The Applicants respectfully disagree, and submit that the cited references, individually or in combination, 1) do not teach, suggest nor enable each element of the amended claims, and 2) actually lead one of ordinary skill in the art away from the claimed invention.

**1) The Cited References, Individually Or In Combination, Do Not Teach or Disclose Each Element of the Amended Claims**

Applicants respectfully submit that the cited references, individually or in combination, fail to teach or disclose all elements of the claims. In particular, currently presented Claim 1 recites, "...[a] composition comprising a dendrimer, said dendrimer comprising a partially acetylated generation 5 (G5) polyamideamine (PAMAM) or polypropylamine (POPAM) dendrimer *wherein greater than 80% of the primary amino groups of said dendrimer are acetylated...*"

None of the cited references describe compositions comprising dendrimers wherein greater than 80% of the primary amino groups of the dendrimer are acetylated. Indeed, the Zhou reference teaches 1) acetylation of only 50% - not greater than 80% - of the primary amino groups of the respective dendrimer (see, Zhou reference at page 251, section 2.4.1), followed by 2) functionalization of the non-acetylated portion of the dendrimer (e.g., the 50% of the dendrimer not acetylated) (see, Zhou reference at page 254-255, section 4)." The Examiner stated that the Applicant must explain the difference between "greater than 80%" and 50% acetylation. Office Action, page 12. The Applicants note that "greater than 80%" versus 50% acetylation results in functionalization differences. For example, functionalization of the Zhou dendrimers can occur on up to 50% of the dendrimer shell while functionalization of the dendrimers recited in currently presented Claim 26 is limited to less than 20% of the dendrimer shell. The Zhou reference appears to depend on highly functionalized dendrimers. It would be counter to the teachings of the Zhou reference to limit the functionality to less than 20%. Likewise, it is not predictable, based on the teachings of the Zhou reference, that a significantly less functionalized dendrimer would remain useful or functional.

As the cited references do not teach or describe all of the elements of currently presented Claim 1, the Applicants request withdrawal of these rejections.

**2) The Cited References Teach Away From the Claimed Invention**

The Applicants respectfully submit that various teachings of Tomalia et al. lead one of ordinary skill in the art away from an acetylated dendrimer defined by Claims 26-46 of the instant application.

The Examiner stated, "Tomalia et al teach ester-terminated PAMAM (G0-G10), hydroxylated terminated PAMA (G0-G9), ketone terminated PAMAM (-NHCOR for G0-G6), and many more (p. 163-167, also see Table 8 on p.165)." (Office Action mailed July 10, 2007, page 4). However, the Examiner fails to acknowledge that the surface reactions disclosed by the Tomalia reference, in addition to being "used in various combinations to create stratified dendrimers with differentiated generations possessing different segment lengths, different branch-juncture multiplicities, and varied hydrophobicity[,]"<sup>1</sup> existed for subsequent functionalization of the dendrimer. In other words, the surface reactions disclosed by Tomalia et al. existed for generating dendrimers with reactive groups for conjugation to other moieties. For example, Tomalia et al. disclose surface reactions of a dendrimer that "can be used to produce linear nonbranched dendrimer segments which possess interior OH groups. Since the OH groups do not participate in Michael addition reactions, these hydroxylated segments can be subsequently functionalized."<sup>2</sup>

Thus, in stark contrast to the Examiner's allegation that Tomalia et al. disclose or suggest an acetylated dendrimer of the present invention, one of ordinary skill in the art immediately appreciates that Tomalia et al. teach dendrimer surface modifications that increase the dendrimer's ability to react with and/or to be conjugated to other moieties (e.g., surrounding compounds). Accordingly, one skilled in the art would not be motivated to acetylate the dendrimer which would inhibit such functionalization.

The Examiner stated, "Tomalia teaches numerous examples of the functionalization of dendrimers of various generations resulting in anionic surfaces, cationic surfaces, chiral surfaces, hydrophobic surfaces, and water-soluble dendrimers (pg. 165, col. 1, lines 6-15) which can be further conjugated to various targeting agents..." Office Action, page 13. Inherent in the passage cited by the Examiner, however, is that the dendrimer functionalized to be water-soluble still retain the ability to be functionalized, which is inconsistent with acetylation. As such, the Tomalia reference teaches away from acetylation, and as such, teaches away from the claimed invention.

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<sup>1</sup> See Tomalia et al., page 164, right column, fourth sentence of the last paragraph beginning on page 164 and continued on page 165.

<sup>2</sup> See Tomalia et al., page 165, left column, lines 1-5.

**III. New Claim 53**

The Applicants present new Claim 53. New Claim 53 is adequately supported in the Specification (see, e.g., the published application at paragraph 249). Claim 53, by being even more restrictive on available functionalization sites, provides additional elements not found in the cited art and is even more taught away from by the prior art.

**CONCLUSION**

All grounds of rejection of the Office Action of September 17, 2008 have been addressed and reconsideration of the application is respectfully requested. It is respectfully submitted that Applicants' claims should be passed into allowance. Should the Examiner believe that a telephone interview would aid in the prosecution of this application Applicants encourage the Examiner to call the undersigned collect at (608) 218-6900.

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